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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application Serial No.:	09/992,832
Applicant:	Adrian Sandler
Filed:	November 16, 2001
Title:	THERAPEUTIC PLACEBO ENHANCEMENT OF COMMONLY-USED MEDICATIONS
TC/A.U.:	1615
Examiner:	Blessing M. Fubara
Attorney Docket No.:	DAS-1

Asheville, North Carolina
January 2, 2004

RESPONSE TO OFFICE ACTION

Date of Deposit: January 2, 2004

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

This is in response to the Office Action of October 2, 2003. Applicant acknowledges that the Examiner reconsidered the restriction requirement with respect to Group I (Claims 1-18) and Group III (Claims 30-41) and has examined the claims of both of those groups. Thus, it is believed that the restriction requirement with respect to Group I (Claims 1-18) and Group III (Claims 30-41) has been withdrawn.

Assuming that the Examiner allows the claims in this Application, Applicant will cancel the claims from Group II (Claims 19-29), the claim from Group IV (Claim 42) and the claims from Group V (Claims 43 and 44) while reserving his right to file a divisional application or divisional applications in an attempt to obtain an allowance of those cancelled claims.

In the Office Action, the Examiner required the Applicant to provide the title, citation and copy of each publication that was a source used for a description of the prior art in the disclosure and a concise explanation of that publication's contribution to the description of prior art.

In the Background of the Invention portion of the Specification, Applicant references an article by Connors, an article by Diamond, and an editorial in the British Medical Journal. On March 11, 2002, Applicant submitted a Supplemental Information Disclosure Statement. The three items are cited on Form PTO-1449. The Connors article is cited as item AO. The Diamond article is cited as item BG. The British Medical Journal editorial is cited as item BL. A copy of each of those articles accompanied the Supplemental Information Disclosure Statement.

The Connors and Diamond articles are relevant prior art because they show that persons with ADHD respond to a placebo when those persons think that the placebo is in fact a stimulant. More specifically, the Connors and Diamond articles are examples of studies of ADHD where the investigators (a) used placebo treatment as a comparison for an active pharmaceutical treatment (not as a form of treatment of ADHD in itself or in combination with an active pharmaceutical); (b) blind the subjects so that they did not know if they were receiving the placebo or the active pharmaceutical; and (c) found that some percentage of the subjects in the experimental trial who received the placebo (and who were blind and therefore did not know that they received a placebo) experienced an improvement in their ADHD symptoms.

Those studies, like the study mentioned in U.S. Patent No. 6,255,325 issued to Dariani, which is cited by the Examiner, do not use the placebo to act as a form of treatment and, instead, only used the placebo as a standard against which to compare treatment with an active pharmaceutical.

The British Medical Journal article recognizes the existence of the placebo effect.

Claims 1-18 and 30-41 were rejected under 35 U.S.C. § 103 as being obvious over U.S. Patent No. 6,255,325 issued to Dariani. The Examiner has taken the position that Dariani discloses a treatment regimen for attention deficit disorder where placebo and methylphenidate are alternated. The Examiner states that Dariani starts out the treatment evaluation with a placebo while Applicant's claims start the treatment with a pharmaceutical. The Examiner also took the position that Applicant made no showing that administering a pharmaceutical first provides unusual results. The Examiner concluded that it would be obvious to one of ordinary skill in the art at the time the invention was made to administer a placebo to a patient in need thereof and then methylphenidate. Applicant respectfully requests that the Examiner reconsider the rejection of Applicant's claims over the Dariani patent.

Applicant's invention, as set forth in independent Claim 1, relates to a method for reducing the normal dosage of a pharmaceutical given to a patient for the treatment of a disorder without substantially reducing effectiveness. The method, as set forth in Claim 1, calls for the administration of an initial dosage of the pharmaceutical during a first predetermined time period. A reduced dosage is administered during a second predetermined time period. The reduced dosage has less pharmaceutical than the initial dosage. The second predetermined time period is subsequent to the first predetermined time period. A placebo is administered during the second predetermined time period, and thus, with the reduced dosage of the pharmaceutical. Applicant's invention should reduce concerns about potential side effects which may result from the use of high doses of pharmaceuticals, such as stimulants like methylphenidate. As shown by the clinical study set forth on pages 11-16 of Applicant's Specification, this method enables children with ADHD to receive fifty percent (50%) of their

normal dose of the stimulant methylphenidate without substantially reducing the effectiveness of the treatment.

U.S. Patent No. 6,255,325 issued to Dariani is directed to the treatment of ADHD and related disorders by the use of an isomer of methylphenidate, namely D-threo methylphenidate instead of the conventional threo racemate of methylphenidate. Dariani has absolutely nothing to do with the treatment of a disorder through the use of a placebo and a reduced dosage of a pharmaceutical as set forth in Applicant's claims. In the Dariani patent, the use of a placebo is discussed in a double blind study to prove the effectiveness of D-threo methylphenidate, as is always done in double or single blind studies. It is certainly well known that a placebo has utility as a standard of comparison in experimental treatment trials, *e.g.,* blinded placebo controlled study wherein subjects either get an active pharmaceutical or a placebo (placebo control) without knowing which they are getting (blind) for the purpose of determining if the active pharmaceutical improves symptoms better than the placebo does. This example of the use of a placebo is restricted to experimental studies and is not an example of using a placebo with a therapeutic intent (as one would use an active pharmaceutical). In using placebos as a comparator in an experimental study, as in the Dariani patent, there is no intent that the placebo will provide therapeutic efficacy.

Dariani simply uses a placebo as one of two forms of comparison conditions for the pharmaceutical that is the subject of his patent claims, namely, D-threo methylphenidate. Dariani also compares his claimed pharmaceutical with threo racemate of methylphenidate, which is the prior art treatment. Dariani does not disclose, discuss or suggest the use of placebos as a form of treatment. In fact, the use of placebo by Dariani implies no treatment by the placebo.

In Column 7 of Dariani, he describes a method used in his study of the D-threo methylphenidate and how it was compared to the racemate drug and to the placebo. Based on his description, over a period of nine days subjects were randomly assigned three different doses of D-threo methylphenidate (three days), three different doses of the racemate (three days), and placebo (two days). On the ninth day, subjects were given whatever treatment they missed. The two day administration of placebo was not for treatment, but are for comparison purposes. In Lines 20-21, Dariani states that a "matching placebo" was used in the study, which means that the placebo pill was made to look like the D-threo methylphenidate and the racemate pharmaceutical pills so that the subject would not know if they were receiving placebo. This is in contrast to one aspect of Applicant's invention, as set forth in Claim 4, whereby the placebo unit has a distinctive indicia.

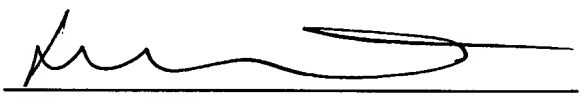
The Dariani patent also includes a statistical analysis of the results of the study provided to support his claims for the use of D-threo methylphenidate. In no instance is anything said about placebo as beneficial treatment of ADD symptoms. Instead, in all of the tables (and the accompanying text that summarizes the tables), a statistical comparison is made regarding the magnitude of the difference between a placebo and two forms of treatment (D-threo methylphenidate or the racemate) in order to determine if the difference exceeds that which would be found by chance. Throughout these sections, Dariani notes that D-threo methylphenidate demonstrates superiority in effectiveness over placebo (*e.g.*, Column 8, Lines 1-2) on particular symptoms of ADD, indicating that placebo condition was used as a comparison for the treatment of the subject of the claimed D-threo methylphenidate. Dariani notes repeatedly that the other form of active treatment (the racemate) that was used as a comparison for the claimed treatment was not superior to the placebo (*e.g.*, Column 9, Line 5).

Applicant's invention, as set forth in independent Claims 1 and 30, calls for treating a patient by first administering a normal dosage of pharmaceutical and then later administering a reduced dosage of pharmaceutical in addition to a placebo. This technique is not suggested by Dariani. In fact, Dariani does not even recognize the problem solved by Applicant's claimed invention.

In summary, Dariani simply uses a placebo based study as a means for proving the effectiveness of a pharmaceutical, which is the case in all such studies. Dariani does not disclose using a placebo to lower the dose of a pharmaceutical, or to use a placebo in combination with another pharmaceutical or treatment, or to use a placebo to augment the effects of another pharmaceutical.

It is therefore respectfully submitted that Dariani does not render Applicant's independent Claims 1 and 30 and their dependent Claims 2-18 and 31-41 obvious. In view of the above, it is believed that this Application is in condition for allowance and an early allowance is solicited.

Respectfully submitted,



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